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EXAMINER	
HILL, KEVIN KAI	

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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/757,345	AGRAWAL ET AL.	
	Examiner	Art Unit	
	Kevin K. Hill, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-146* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-146* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Claim 27 has been cancelled by the Applicant.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 3, 5, 7-16, 18 and 31, drawn to an immunomer compound comprising at least two oligonucleotides linked together, classified in class 514, subclass 44.

II. Claims 2, 4, 6, 19-26, 28 and 30, drawn to an immunomodulatory oligonucleotide comprising an immunostimulatory dinucleotide, classified in class 514, subclass 44.

III. Claim 17, drawn to an immunomer conjugate comprising an immunomer compound comprising at least two oligonucleotides linked together and an antigen conjugated to the immunomer at a position other than the accessible 5' end, classified in class 514, subclass 44.

IV. Claim 29, drawn to an immunomodulatory conjugate comprising an immunomodulatory oligonucleotide compound comprising an immunostimulatory dinucleotide and an antigen conjugated to the immunomer at a position other than the accessible 5' end, classified in class 514, subclass 44.

V. Claims 56, drawn to an immunostimulatory oligonucleotide comprising two or more oligonucleotide segments covalently linked 5' to 3' by a non-nucleotidic linker, classified in class 514, subclass 44.

VI. Claims 57-102, drawn to an immunomer comprising at least two oligonucleotides linked together, wherein at least one of the oligonucleotides is an immunostimulatory oligonucleotide comprising an immunostimulatory dinucleotide and, optionally, an immunostimulatory moiety, classified in class 514, subclass 44.

VII. Claims 103-127, drawn to an immunomodulatory oligonucleotide comprising an immunostimulatory dinucleotide and, optionally, an immunostimulatory moiety, classified in class 514, subclass 44.

VIII. Claims 32 and 40-42, drawn to a method for generating an immune response in a vertebrate, the method comprising administering to the vertebrate an immunomer compound comprising at least two oligonucleotides linked together and a vaccine, classified in class 514, subclass 44.

IX. Claim 33, drawn to a method for generating an immune response in a vertebrate, the method comprising administering to the vertebrate an immunomer conjugate comprising an immunomer compound comprising at least two oligonucleotides linked together and an antigen conjugated to the immunomer at a position other than the accessible 5' end, classified in class 514, subclass 44.

X. Claims 34-35, drawn to a method for therapeutically treating a patient having a disease or disorder, comprising administering to the patient an immunomer compound comprising at least two oligonucleotides linked together, classified in class 514, subclass 44.

XI. Claims 36 and 38, drawn to a method for therapeutically treating a patient having a disease or disorder, comprising administering to the patient an immunomer conjugate comprising an immunomer compound comprising at least two

oligonucleotides linked together and an antigen conjugated to the immunomer at a position other than the accessible 5' end, classified in class 514, subclass 44.

XII. Claims 37 and 39, drawn to a method for therapeutically treating a patient having a disease or disorder, comprising administering to the patient an immunomer compound comprising at least two oligonucleotides linked together, classified in class 514, subclass 44.

XIII. Claim 43, drawn to a method for generating an immune response in a vertebrate, the method comprising administering to the vertebrate an immunomodulatory oligonucleotide comprising an immunostimulatory dinucleotide, classified in class 514, subclass 44.

XIV. Claim 44, drawn to a method for generating an immune response in a vertebrate, the method comprising administering to the vertebrate an immunomodulatory conjugate comprising an immunomodulatory oligonucleotide compound comprising an immunostimulatory dinucleotide and an antigen conjugated to the immunomer at a position other than the accessible 5' end, classified in class 514, subclass 44.

XV. Claims 45-46, drawn to a method for therapeutically treating a patient having a disease or disorder, comprising administering to the patient an immunomodulatory oligonucleotide comprising an immunostimulatory dinucleotide, classified in class 514, subclass 44.

XVI. Claims 47 and 49, drawn to a method for therapeutically treating a patient having a disease or disorder, such method comprising administering to the patient an immunomodulatory conjugate comprising an immunomodulatory oligonucleotide compound comprising an immunostimulatory dinucleotide and an antigen

conjugated to the immunomer at a position other than the accessible 5' end, classified in class 514, subclass 44.

XVII. Claims 48, 50 and 54-55, drawn to a method for therapeutically treating a patient having a disease or disorder, such method comprising administering to the patient an immunomodulatory oligonucleotide comprising an immunostimulatory dinucleotide, wherein the immunostimulatory dinucleotide has the structure of Formula II, classified in class 514, subclass 44.

XVIII. Claims 128-136, drawn to a method for therapeutically treating a patient having a disease or disorder, such method comprising administering to the patient an immunomer comprising at least two oligonucleotides linked together, wherein at least one of the oligonucleotides is an immunostimulatory oligonucleotide comprising an immunostimulatory dinucleotide and, optionally, an immunostimulatory moiety, classified in class 514, subclass 44.

XIX. Claims 137-139, drawn to a method for the prophylactic treatment of a patient to prevent the onset of a disease or disorder, such method comprising administering to the patient an immunomodulatory oligonucleotide comprising an immunostimulatory dinucleotide and, optionally, an immunostimulatory moiety, classified in class 514, subclass 44.

XX. Claims 140-146, drawn to a method for the prophylactic treatment of a patient to prevent the onset of a disease or disorder, such method comprising administering to the patient an immunomer compound comprising at least two oligonucleotides linked together, a vaccine and another therapeutic agent, classified in class 514, subclass 44.

Inventions I-VII are directed to related products. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the Groups III-IV compositions further comprise an antigen; whereas, Groups I-II and V-VII do not. Furthermore, the Groups I-IV compositions are of the structural Formula III and the oligonucleotide sequences are undisclosed; whereas, the Groups V-VII compositions are not of the structural Formula III, and in the case of Groups VI-VII also disclose an oligonucleotide of specific sequence. The Groups I, III and VI oligonucleotides are linked at their 3' ends; whereas, the Group V oligonucleotides are linked 5' to 3' by a non-nucleotidic linker, and the Groups II, IV and VII oligonucleotides do not recite a specific covalent linkage orientation.

A search for an immunomer compound comprising at least two oligonucleotides linked together would not be co-extensive with a search for an immunomodulatory conjugate comprising an immunomodulatory oligonucleotide compound comprising an immunostimulatory dinucleotide and an antigen conjugated to the immunomer at a position other than the accessible 5' end. Further, a reference rendering an immunomer compound comprising at least two oligonucleotides linked together as anticipated or obvious over the prior art would not necessarily also render an immunomodulatory conjugate comprising an immunomodulatory oligonucleotide compound comprising an immunostimulatory dinucleotide of a specific SEQ ID NO as anticipated or obvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Inventions VIII-XX are directed to related processes. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use

together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, each of the inventive methods are performed using distinctly different products, as described above, and thus are materially different in design, mode of operation and effect. For example, the Groups VIII-IX and XIII-XIV methods are designed to generate an immune response; whereas Groups XIX-XX are designed to prevent a disease or disorder, and Groups X-XII and XV-XVIII are designed to treat a patient suffering from a disease or disorder. Furthermore, the disease and disorder pathologies are etiologically and symptomatically different, contain different process steps and effect different endpoints, such that each treatment will be targeted to different tissues and cells, and are not disclosed as capable of use together.

A search for a method for generating an immune response in a vertebrate would not be co-extensive with a search for a method for therapeutically treating a patient having a disease or disorder. Further, a reference rendering a method for the prophylactic treatment of a patient to prevent the onset of a disease or disorder as anticipated or obvious over the prior art would not necessarily also render a method for therapeutically treating a patient having a disease or disorder as anticipated or obvious over the prior art. Similarly, a finding that a method for the prophylactic treatment of a patient to prevent the onset of a disease or disorder was novel and unobvious over the prior art would not necessarily extend to a finding that a method for generating an immune response in a vertebrate was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Inventions I-VII and VIII-XX are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the breadth of the recited oligonucleotides,

internucleoside linkages, modified purine derivatives and optional secondary agents demonstrates that the Groups VIII-XX methods may be practiced with materially and structurally independent and distinct products.

A search for an immunomer compound comprising at least two oligonucleotides linked together would not be co-extensive with a search for a method for therapeutically treating a patient having a disease or disorder. Further, a reference rendering a method for generating an immune response in a vertebrate as anticipated or obvious over the prior art would not necessarily also render an immunomer conjugate comprising an immunomer compound comprising at least two oligonucleotides linked together and an antigen conjugated to the immunomer at a position other than the accessible 5' endas anticipated or obvious over the prior art. Similarly, a finding that an immunomodulatory oligonucleotide comprising an immunostimulatory dinucleotide and, optionally, an immunostimulatory moiety was novel and unobvious over the prior art would not necessarily extend to a finding that a method for the prophylactic treatment of a patient to prevent the onset of a disease or disorder was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper

restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

2. **Should Applicant elect any of Invention(s) I-IV or VIII-XVII or XX, a further group restriction is required under 35 U.S.C. 121.** Claim(s) 1 and 2 are generic to an immunomer composition. Applicant is required to elect a single disclosed immunomer composition further comprising a secondary agent recited specifically in Claim(s) 7-8 and 19-21 for prosecution on the merits to which the claims shall be restricted. Therefore, election is required of Invention I and one of Invention I, inventive groups (a)-(d) below, specifically:

a) one oligonucleotide that is complementary to a gene, as recited in Claims 7 and 19,

b) one ribozyme, as recited in Claims 8 and 20,

c) one decoy oligonucleotide, as recited in Claims 8 and 20, or

d) one Nn portion that includes a G3-G10 region, as recited in Claims 9 and 21.

Claims 1 and 2 link inventive groups (a)-(d).

Inventive groups (a)-(d) are distinct because,

Inventive groups (a)-(d) are unrelated. The secondary agents are independent and structurally distinct compositions whose mode of operation(s) are distinctly different. For example, a ribozyme effects its gene-silencing properties by a distinctly different mechanism than an oligonucleotide that is complementary to a gene.

A search for an oligonucleotide that is complementary to a gene would not be co-extensive with a search for a Nn portion that includes a G3-G10 region. Further, a reference

rendering a ribozyme as anticipated or obvious over the prior art would not necessarily also render a decoy oligonucleotide as anticipated or obvious over the prior art. Similarly, a finding that one oligonucleotide was novel and unobvious over the prior art would not necessarily extend to a finding that another oligonucleotide was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed immunomer composition further comprising a secondary agent, even though this requirement is traversed. Failure to elect an immunomer composition further comprising a secondary agent from inventive groups (a)-(d) above consonant with Applicant's elected Invention, may result in a notice of non-responsive amendment.

Claims 1 and 2 link inventive groups (a)-(d). The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), Claims 1 and 2. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim(s) including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

3. **Should Applicant elect any of Inventions I-IV, VIII-XVII or XX, a species election is required under 35 USC 121.** Currently, Claims 1 and 2 of this application is directed to a plurality of disclosed, patentably distinct "G" moieties of the immunostimulatory dinucleotide having the structure of RpG that prohibit proper examination of these claims. Therefore, election is required under 35 U.S.C. 121 of one "G" radical moiety from the list consisting of the "G" radical moieties recited in Claims 1-2, 18 and 30, consonant with Applicant's elected invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

In the instant case, each species is independent and structurally distinct. The numerous variations in the number, position and type of heteroatoms result in a vast genus of structurally unrelated molecules that are not obvious variations of each other because one skilled in the art does not expect a guanosine to have the same chemical properties as a 2'-O-substituted arabinoguanosine, for example. Each of the radical species moieties confers a unique, non-obvious property onto the modified nucleoside derivative that will directly impact the bioavailability, toxicity or bioactivity of the compound. Given the breadth of the claimed, unrelated structures, a search for all possible species at each of the recited radical groups imposes an exceptional burden on the Office.

A search for guanosine would not be co-extensive with a search for a non-natural purine nucleoside. Further, a reference rendering 2'-deoxyguanosine as anticipated or obvious over the prior art would not necessarily also render 2'-O-substituted-arabinoguanosine as anticipated or obvious over the prior art. Similarly, a finding that one non-natural purine nucleoside was novel and unobvious over the prior art would not necessarily extend to a finding that another non-natural purine nucleoside was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed "G" moiety species of the immunostimulatory dinucleotide having the structure of RpG, even though this

requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect a "G" moiety species consonant with Applicant's elected invention may result in a notice of non-responsive amendment.

Should Applicant elect any of Inventions I, III, VIII-XII or XX, a species election is required under 35 USC 121. Currently, Claim 1 of this application is directed to a plurality of disclosed, patentably distinct oligonucleotide linkages that prohibit proper examination of this claim. Therefore, election is required under 35 U.S.C. 121 of one oligonucleotide linkage from the list consisting of the oligonucleotide linkages recited in Claim 1 consonant with Applicant's elected invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable, specifically:

i) linkage at the 3' end,

ii) an internucleoside linkage,

iii) a functionalized nucleobase, or

iv) a sugar to a non-nucleotidic linker.

In the instant case, each oligonucleotide linkage species is independent and structurally distinct. Each oligonucleotide linkage confers a unique, non-obvious property onto the modified, immunostimulatory oligonucleotide that are not obvious variations of each other because one skilled in the art does not expect oligonucleotide linkages at the 3' end to have the same chemical properties as an oligonucleotide linkage consisting of a sugar to a non-nucleotidic linker. Given the breadth of the claimed, unrelated structures, a search for all possible species at each of the oligonucleotide linkage imposes an exceptional burden on the Office.

A search for an internucleoside linkage would not be co-extensive with a search for a functionalized nucleobase. Further, a reference rendering a linkage at the 3' end as anticipated or obvious over the prior art would not necessarily also render a functionalized nucleobase as

anticipated or obvious over the prior art. Similarly, a finding that a sugar to a non-nucleotidic linker was novel and unobvious over the prior art would not necessarily extend to a finding that an internucleoside linkage was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed oligonucleotide linkage species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect an oligonucleotide linkage species consonant with Applicant's elected invention may result in a notice of non-responsive amendment.

Should Applicant elect any of Inventions I-IV, VIII-XVII or XX, a species election is required under 35 USC 121. Currently, Claims 3 and 4 of this application is directed to a plurality of disclosed, patentably distinct oligonucleotides of Formula III, 5'-Nn-N1-Y-Z-N1-Nn-3', that prohibit proper examination of these claims. Therefore, election is required under 35 U.S.C. 121 of one "N1" radical at each occurrence, one "Nn" radical at each occurrence, and one "Z" radical from their respective Markush Groups recited in Claims 3-6 consonant with Applicant's elected invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

It is noted that if Applicant elects the "immunostimulatory moiety" of Claims 3 and 4 to be a nucleoside linked by a modified internucleoside linkage to the adjacent nucleoside on the 3' side, then a further species election is required of the corresponding Markush Group of modified internucleotide linkages recited in Claims 3 and 4.

In the instant case, each species is an independent and structurally distinct oligonucleotide composition. The numerous variations in the number, position and type of heteroatoms, ring structures, and linear carbon chains result in a vast genus of structurally unrelated molecules that are not obvious variations of each other because one skilled in the art does not expect an arabinonucleoside to have the same chemical properties as 2'-deoxyuridine. Similarly, one skilled in the art does not expect a polyethyleneglycol internucleotide linkage to have the same chemical properties as a phosphorodithioate linkage. Each of the radical species moieties confers a unique, non-obvious property onto the modified immunostimulatory moiety that will directly impact the bioavailability, toxicity or bioactivity of the compound. Given the breadth of the claimed, unrelated structures, a search for all possible species at each of the recited radical groups imposes an exceptional burden on the Office.

A search for one possible oligonucleotide structure would not necessarily be co-extensive with a search for another possible oligonucleotide structure. Further, a reference rendering one possible oligonucleotide structure as anticipated or obvious over the prior art would not necessarily also render another possible oligonucleotide structure as anticipated or obvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed oligonucleotide composition species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect an oligonucleotide composition species consonant with Applicant's elected invention may result in a notice of non-responsive amendment.

Should Applicant elect any of Inventions I-IV, VIII-XVII or XX, a species election is required under 35 USC 121. Currently, Claims 10-14 and 22-26 of this application are directed to a plurality of disclosed, patentably distinct modified purine nucleosides of the structure of Formula II in the immunostimulatory or immunomodulatory oligonucleotide that prohibit proper examination of these claims. Therefore, election is required under 35 U.S.C. 121 of one "D" hydrogen bond donor, one "D prime" moiety, one "A" moiety, one "X" moiety, one "L" moiety and one "S prime" moiety, from their respective lists, as recited in Claims 11-14, for example, consonant with Applicant's elected invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

In the instant case, each modified purine nucleoside species is independent and structurally distinct. The numerous variations in the number, position and type of heteroatoms, ring structures, and non-naturally occurring purine compounds result in a vast genus of structurally unrelated molecules that are not obvious variations of each other because one skilled in the art does not expect carbon heteroatoms to have the same chemical properties as sulphur heteroatoms, for example. Similarly, one skilled in the art would not expect a pentose ring to have the same chemical properties as 6-oxopurine. Each of the radical species moieties confers a unique, non-obvious property onto the modified nucleoside derivative that will directly impact the bioavailability, toxicity or bioactivity of the compound. Given the breadth of the claimed, unrelated structures, a search for all possible species at each of the recited radical groups imposes an exceptional burden on the Office.

A search for one possible modified purine nucleoside structure would not be co-extensive with a search for another possible modified purine nucleoside structure. Further, a reference rendering one possible modified purine nucleoside structure as anticipated or obvious over the prior art would not necessarily also render another possible modified purine nucleoside structure as anticipated or obvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed modified purine nucleoside structure species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect a modified purine nucleoside structure species consonant with Applicant's elected invention may result in a notice of non-responsive amendment.

Should Applicant elect any of Inventions I, III, VIII-XII or XX, a species election is required under 35 USC 121. Currently, Claim 15 of this application is directed to a plurality of disclosed, patentably distinct non-nucleotidic linkers that prohibit proper examination of this claim. Therefore, election is required under 35 U.S.C. 121 of one non-nucleotidic linker from the list consisting of the non-nucleotidic linkers recited in Claim 15 consonant with Applicant's elected invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

In the instant case, each species is independent and structurally distinct. The numerous variations in the number, position and type of heteroatoms, ring structures, and linear or branched carbon chains result in a vast genus of structurally unrelated molecules that are not obvious variations of each other because one skilled in the art does not expect aromatic ring systems to have the same chemical properties as non-aromatic ring systems. Each of the radical species moieties confers a unique, non-obvious property onto the non-nucleotidic linker, and thus the immunostimulatory oligonucleotide that will directly impact the bioavailability, toxicity or bioactivity of the compound. Given the breadth of the claimed, unrelated structures, a search for all possible species at each of the recited radical groups imposes an exceptional burden on the Office.

A search for a metal linker would not be co-extensive with a search for a biomolecule linker. Further, a reference rendering an aromatic hydrocarbon with an amino acid functional group as anticipated or obvious over the prior art would not necessarily also render a

biodegradable polymer bead as anticipated or obvious over the prior art. Similarly, a finding that an acyclic small molecule was novel and unobvious over the prior art would not necessarily extend to a finding that a hydrocarbon appended with cholesterol was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed non-nucleotidic linker species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect a non-nucleotidic linker species consonant with Applicant's elected invention may result in a notice of non-responsive amendment.

Should Applicant elect any of Inventions VI-VII or XVIII-XIX, a species election is required under 35 USC 121. Currently, Claims 57, 103, 128 and 137 of this application are generic to a plurality of disclosed patentably distinct species comprising immunostimulatory oligonucleotides of patentably distinct SEQ ID NO's that prohibit proper examination of these claim. Therefore, election is required under 35 U.S.C. 121 of one immunostimulatory oligonucleotide of a patentably distinct SEQ ID NO from the respective lists consisting of the SEQ ID NO's recited in Claims 58-102, 104-127, 130-136 and 139 consonant with Applicant's elected invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Each of the immunostimulatory oligonucleotide species is independent and structurally distinct. Applicants are reminded that nucleic acid sequences are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent

evidence to the contrary, each such nucleic acid is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

Given the breadth of the claimed, unrelated structures, a search for all possible species at each of the recited immunostimulatory oligonucleotides imposes an exceptional burden on the Office. A search for SEQ ID NO: 3 would not be co-extensive with a search for SEQ ID NO: 31. Further, a reference rendering SEQ ID NO: 134 as anticipated or obvious over the prior art would not necessarily also render SEQ ID NO: 114 as anticipated or obvious over the prior art. Similarly, a finding that immunostimulatory oligonucleotide of a patentably distinct SEQ ID NO was novel and unobvious over the prior art would not necessarily extend to a finding that another immunostimulatory oligonucleotide of a patentably distinct SEQ ID NO was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed one immunostimulatory oligonucleotide of a patentably distinct SEQ ID NO, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect an immunostimulatory oligonucleotide of a patentably distinct SEQ ID NO consonant with Applicant's elected Invention, may result in a notice of non-responsive amendment.

Should Applicant elect any of Inventions VIII, XI-XII or XV-XX, a species election is required under 35 USC 121. Currently, Claims 34, 36-37, 45, 47-48, 128, 137 and 140 of this application are generic to a plurality of disclosed patentably distinct disease and disorder species

that prohibit proper examination of these claims. Therefore, election is required under 35 U.S.C. 121 of one disease or disorder from the respective lists consisting of the diseases or disorders recited in Claims 35, 38-39, 46, 49-50, 129, 138 and 141 consonant with Applicant's elected invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Each disease and disorder is unrelated, as they are etiologically and symptomatically different. A cancerous disease is distinctly different from an allergy, for example. The different invention(s) are designed to treat patients with independent and distinct disease pathologies, contain different process steps and effect different endpoints, such that each treatment will be targeted to different tissues and cells.

A search for cancer would not be co-extensive with a search for asthma. Further, a reference rendering a skin disorder as anticipated or obvious over the prior art would not necessarily also render a disease caused by a pathogen as anticipated or obvious over the prior art. Similarly, a finding that airway inflammation was novel and unobvious over the prior art would not necessarily extend to a finding that an autoimmune disorder was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed disease or disorder species, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect a disease or disorder species consonant with Applicant's elected invention may result in a notice of non-responsive amendment.

Should Applicant elect any of Inventions XVII or XX, a species election is required under 35 USC 121. Currently, Claims 54, 140 and 145 of this application are generic to a plurality of disclosed patentably distinct species comprising therapeutic agents that prohibit proper examination of these claims. Therefore, election is required under 35 U.S.C. 121 of one therapeutic agent from the list consisting of the agents recited in Claims 55 and 146 consonant with Applicant's elected invention for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Each therapeutic agent species is independent and distinct, is mutually exclusive of the others yields distinctly different effects made manifest by a distinctly different mode of action. The large genus of structurally unrelated molecules are not obvious variations of each other because one skilled in the art does not expect an antibody to have the same biological properties as a chemotherapeutic agent.

A search for an antibody would not be co-extensive with a search for a chemotherapeutic agent. Further, a reference rendering a vaccine as anticipated or obvious over the prior art would not necessarily also render an antibody as anticipated or obvious over the prior art. Similarly, a finding that an allergen was novel and unobvious over the prior art would not necessarily extend to a finding that an antibiotic was also novel and unobvious over the prior art. Because these inventions are distinct for reasons given above, and because a search of one does not necessarily overlap with that of another species, it would be unduly burdensome for the examiner to search and examine all the subject matter being sought in the presently pending claims and thus, restriction for examination purposes as indicated is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed therapeutic agent, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election. Failure to elect a therapeutic agent consonant with Applicant's elected Invention, may result in a notice of non-responsive amendment.

Should Applicant traverse on the ground that the species are not patentably distinct, Applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER